COMMENTARY

Mechanisms, Proof, and Unmet Needs: The Perspective of a Cancer Activist

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Cancer activists who participate with cancer researchers in shaping public health policy provide a different perspective on the question of breast cancer etiology. We place a higher priority on reducing women's exposure to suspected breast carcinogens than in debating the specific biochemical mechanisms by which these agents may operate. As the fruits of AIDS activism and antismoking campaigns illustrate, answers to mechanistic questions have not been and should not be the driving force behind public health policy. As such, cancer activists embrace a form of conservatism that advocates prudence in the face of exposure to estrogenic and other endocrine-disrupting chemicals. This perspective stands in contrast to scientific conservatism, which directs its caution toward the issue of proof. Unmet needs for cancer activists refer not so much to data gaps as to the failure to eliminate ongoing cancer hazards. For this author and activist, unmet needs include ending women's continued exposure to such common estrogenic compounds as detergents, triazine herbicides, plastics, and polychlorinated biphenyls. — *Environ Health Perspect* 105(Suppl 3):685–687 (1997)

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When we in the cancer activist community look at breast cancer research, we are interested not only in results, sample size, elegance of experimental design, or validity of the conclusions based on the data. We are also interested in—and are most interested in—saving women's lives. Therefore, we are interested in understanding how particular lines of scientific inquiry are chosen for funding and intellectual pursuit, and we are interested in influencing those choices. We are interested in how public health policy is made in the face of scientific uncertainty. We are interested in research that identifies breast carcinogens, and we are interested in social changes that could keep those agents out of women's breasts in the first place. In short, when researchers and activists meet (for example, as members of the National Action Plan on Breast Cancer [NAPBC]), activists bring to the table a particular perspective on the role of science, the direction it travels, and its methodologies.

Consider the issue of unmet needs, which members of the NAPBC's etiology working group are requested to address. To a scientist, an unmet need may represent a data gap within his or her area of expertise. To an activist, an unmet need may refer to life without a breast cancer diagnosis. In the context of estrogenic chemicals and their relationship to breast cancer, I have my own personal list of unmet needs.

Learning how to clean clothes without the use of estrogenic detergents is an unmet need. Household detergents, as well as paints and pesticides, contain estrogenic alkylphenol polyethoxylates (APEOs). Since their introduction as chemical surfactants in the 1940s, APEOs have become widely disseminated in rivers, lakes, and streams, and therefore in drinking water. In 1994, researchers in England discovered that APEOs, in trace amounts, can stimulate the growth of breast cancer cells (*1*).

Finding ways to keep weeds out of corn fields without the use of triazine herbicides is an unmet need. Classified as a possible human carcinogen, the chloroplast-destroying triazines have been used since the 1950s. They have been detected in raindrops in 23 states in the upper Midwest and northeast United States, including pristine areas such as Isle Royale National Park in northern Minnesota, and they gain entry into our bodies as contaminants of drinking water and as residues on food. At least one of the triazines, atrazine, is a known endocrine disrupter and is restricted for use in Germany, the Netherlands, and several Nordic countries. However, in the United States, atrazine is used on about 73% of all corn fields. Atrazine causes mammary gland cancer in at least one strain of laboratory rat (*2*). It also causes chromosomal breakage in the tissues of hamster ovaries at concentrations below its maximum legal limit in drinking water (*3*). Case–control studies in northern Italy show a connection between exposure to triazine herbicides and ovarian cancer among women farmers (*4,5*). Triazine weed killers in the Corn Belt states where I grew up can reach breathtaking levels in rivers and streams, and in the finished drinking water drawn from these sources, during the spring months of planting and rain (*6*).

Discovering substitutes for polyvinyl chloride (PVC) plastic is an unmet need. Vinyl chloride, the industrial feedstock of PVC, is considered a known human carcinogen because of its link to a rare form of liver cancer (*7*). A 1977 study showed that women who breathe vinyl chloride vapors on the job showed a 36% excess in breast cancer mortality (*8*). Inhalation of vinyl chloride as well as ingestion of PVC dust triggers breast cancer in female rats even at the lowest doses (*9*). Freshwater fish contain residues of vinyl chloride as does drinking water, both because vinyl chloride is a frequent contaminant of groundwater and because PVC water pipes can shed vinyl chloride from their interior surfaces. Vinyl chloride vapors also waft from hazardous waste sites and are an important air pollutant (*7,10*). It is time to phase out vinyl chloride.

PVC also contains phthalate plasticizers, which demonstrate estrogenic properties. Traces of phthalates can be found in food where, like vinyl chloride monomers, they have migrated from their plastic packaging (*11*). Ironically, women cancer patients may have higher exposures to vinyl chloride and phthalates than the general

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Abbreviations used: APEOs, alkylphenol polyethoxylates; NAPBC, National Action Plan on Breast Cancer; PCBs, polychlorinated biphenyls; PVC, polyvinyl chloride.

population; hospitals are full of PVC products, including the equipment used for blood transfusions and intravenous drips. Are cancer patients receiving breast carcinogens by direct entry into the bloodstream even as they are being treated for their disease? Recent interest in developing a healthy hospitals campaign that would address such issues is circulating among cancer activists and progressive health care professionals.

A plan to recall, recapture, and contain polychlorinated biphenyls (PCBs) is an unmet need. Invented in 1929 and banned in 1978, PCBs are the elders of the synthetic organochlorine family. Preliminary research has linked these electrical insulators to breast cancer, and wildlife research reveals their potential for endocrine disruption (*12*). When painted on the eggs of certain turtle species, PCBs turn male embryos into females. Moreover, they have the power to do so at very low concentrations—levels that are comparable to the average level of PCBs now found in the breast milk of women living in industrialized countries (*13*). Of the 209 possible PCB configurations, some appear to be estrogenic and some not. We could decide to funnel resources toward deciphering which congeners belong in which category, or we could decide to fund a campaign to recapture them, thus preventing additional PCBs from entering our food chain. Only about one-third of the world's total production of PCBs is believed to have escaped into the general environment. Like thousands of tiny bombs exploding in slow motion, pieces of discarded equipment containing the oily fluid (electrical transformers, television sets, old french fryers) leak their contents drop by drop into the soil and water. From there, PCB molecules rise into the atmosphere, circulate with the wind, and are redeposited all over the globe. They then enter the food chain (*14,15*). We could very well save more women's lives by allocating money to get PCBs out of landfills than we could by continuing to debate the specific pathways by which estrogenic chemicals such as PCBs are metabolized. The impossibility of quantifying the precise numbers of breast cancer deaths due to PCBs, or any other suspected breast carcinogen, should not deter us from the task. Recognizing that cancer is a multicausal disease with interlocking risk factors, breast cancer activists follow ecologist Rachel Carson's lead in arguing that a substantial reduction in the total load of chemical carcinogens to which we are all exposed would prevent considerable numbers of cancer diagnoses and cancer deaths (*16*).

This brings me to the issue of mechanisms and proof. The NAPBC, it seems to me, spends a great deal of time and energy on the topic of genetic and biochemical mechanisms of carcinogenesis. While I am as fascinated as any other biologist at the exquisite nexus of interactions among chemical metabolites, cellular receptors, and DNA, I contend that public health policy has not and should not be driven by the answers to mechanistic questions. When we become concerned about handgun violence in the cities in which we live, we do not need to understand everything about the ballistics of bullets in order to take preventive action. When we become concerned about children's exposure to lead, we do not need to describe every link in the biochemical chain between blood levels and lowering of IQ in order to demand an end to lead additives in gasoline and a remediation of lead-based paint in housing. When we need to protect ourselves against AIDS, we do not need to know everything about CD4 receptor molecules or cofactor fusin proteins before learning how to use condoms. Indeed, safe sex education and needle exchange dramatically lowered HIV infection rates among certain key populations years before scientists identified the mechanisms by which the AIDS virus gains entry into human immune cells. Thousands more lives would have been lost had we waited to take action until all the viral mechanisms of infection were elucidated. Breast cancer prevention efforts need to take a lesson from the successes of AIDS activism. (Ironically, the focus on AIDS prevention has been facilitated in part by the incurable nature of the disease. By contrast, breast cancer prevention efforts have historically been overshadowed by the glamor of seeking a cure, and more recently, by the fatalistic focus on early detection.)

The issue of mechanisms is closely allied with the issue of proof. Here, scientists and activists bring two different types of conservatism to the topic of cancer research. As argued brilliantly by science historian Robert Proctor, scientists are conservative when they take care not to overestimate a hazard or when they speak cautiously when making statements of fact. What is being conserved here is the existing body of scientific knowledge, as well as the reputation of the speaker. Cancer activists, on the other hand, tend to embrace the brand of conservatism practiced within the field of public health: prudence for us means acting to reduce cancer hazards even in the face of incomplete scientific knowledge. In the words of Proctor, "to do otherwise, to wait and see, to delay in the face of good but partial evidence, is tantamount to experimenting on humans" (*17*).

This second definition of conservatism was certainly the driving force behind the decision to criminalize secondhand smoke. Of the 30 studies investigating its connection to lung cancer, only 9 showed statistically significant risks; 6 showed no risk at all or negative risks. Despite the negative studies and despite the fact that the mechanisms behind tobacco's ability to cause lung cancer are still not well understood, the U.S. Environmental Protection Agency declared environmental tobacco smoke a known human carcinogen (*18*). Changes in public policy quickly followed. Tireless efforts by antismoking activists played as much a role in codifying our right to smoke-free airplanes, restaurants, hospitals, and work places as the results of scientific study.

Many breast cancer activists have been inspired by this kind of weight-of-the-evidence approach to environmental health problems. In considering what kind of criteria should be used for regulating known and suspected breast carcinogens, we are additionally inspired by a key principle that has emerged from the field of environmental ethics. This is the precautionary principle, which dictates that indication of harm, rather than proof of harm, should be the trigger for action (*19*). By contrast, our current system of regulation appears governed by what some of us have referred to as "the dead body approach," which waits until damage is proven before action is taken.

"'We need more study' is the grandfather of all arguments for taking no action," warns Peter Infante, director of the Health Standards Program at the Occupational Safety and Health Administration (*20*). As we go forward, activists and scientists together, we must debate the question of what constitutes sufficient evidence to advocate public health action even as we advocate for more research into the question of how exactly the metabolism of endogenous estrogens and xenoestrogenic chemicals contributes to rising breast cancer incidence (*21*).

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